REMARKS

It is recognized, now, that the original disclosure and claims actually spanned a set of three inventive formulations. To better differentiate the benefits and applications of each some divisional continuation-in-part applications would appear to be a best approach. The current claims have been narrowed to deal with the novel formulation which permits high stability for liposomes during freeze-drying and reconstitution. As such the specification warrants the use of monosaccharides together with synthetic phospholipids and a non-polar porphyrin type photosensitizer to create a formulation which is stable through these processes and can be effectively used in a PDT treatment.

Note that currently claim 3 is withdrawn/cancelled as going to a no-longer elected invention. Claims 15 and 16 are likewise cancelled/withdrawn. Claims 1, 2 were amended for content, while changes to other claims reflect the amendments to claims 1 and 2. The set of claims open for prosecution are thus claims 1, 2, 6, 8, 10, 11 and 13.

Claim Rejections- 35 USC § 112 para. 2

Applicant submits that the currently amended claims are covered in sufficient detail in the specification for one skilled in the art of porphyrin formulation to appreciate and follow.

Briefly, as described in the amended claims, the liposomal formulation of the present invention consists substantially of phospholipids and a therapeutically effective amount of a non-polar di- or tetrahydro porphyrin derivative. and one or more monosaccharides or polyalcohols. The specific names for di-hydro porphyrin and tetra-hydro porphyrin, chlorin and bacteriochlorin respectively, were removed from amended claim 1. Further the restriction of claim 5 was brought into amended claim 1 and adjustments made to the claim set to reflect this.

Claim Rejections – 35 USC § 103

As recited in MPEP 2143 *et seq.*, to establish a *prima facie* case of obviousness, three basic criteria must be met:

(1) There must be some suggestion or motivation to modify the teachings of the reference.

(2) There must be a reasonable expectation of success.

(3) The references must teach or suggest all the claim limitations.

Claims 1-2, 5 and 9 to 14 were rejected as being unpatentable over Desai et al. in US 6,074,666 ('666) and over Madden in US 5,389,378 ('378).

The *prima facie* case of obviousness has not been established with respect to '666 in view of '378 because the references do not disclose all of the elements of the present invention as set out in the claims nor do the references suggest, teach, or imply a motivation to combine the reference teachings in order to produce the present invention. Furthermore, despite '378 teaching the use of a variety of sugars, including monosaccharides, both cited references reject the use of monosaccharides in porphyrin-derivative liposome formulations. Instead, both references indicate that certain desirable characteristics either would be hindered or precluded with the use of monosaccharides in a porphyrin-liposome formulation. Neither reference has given any indication that monosaccharides will protect any phospholipid liposomal formulation containing a non-polar photosensitizer during freeze-drying and reconstitution. In fact actual testing has revealed that with many phospholipids the reconstituted formulation with monosaccharide rather come back as agglomerated vesicles with a broad range of sizes, and thus would not be successfully introduced systemically. As a result, neither of the cited references, nor the combination of the two, create a reasonable expectation of success regarding the use of monosaccharides in a porphyrin-derivative liposome formulation. For these reasons, Applicants respectfully submit that the present invention is patentable over the cited references.

Contrary to the reference teachings, Applicants' formulation may contain between 2-12% monosaccharide, as shown in example 1c on page 8 of the present application. Moreover, in direct contrast to the teachings of '666, Applicants' formulations also had a

mean particle size below 200 nm, namely, 166 nm, and were found to function well. (Present application, page 8)

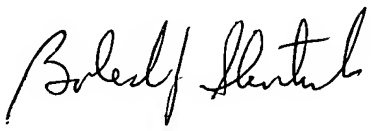
Clearly, both references advocate against the use of monosaccharides in order to achieve and maintain a storage-stable liposome with a reproducible and desirable particle size. Accordingly, the reference teachings do not create a reasonable expectation of success that a formulation having a particle size less than 200 nm would result from a liposome having at least one Pegylated phospholipid and one or more monosaccharides or polyalcohols. Moreover, the combination of these two references do not encompass each and every element of the present invention. For these reasons, the present invention is patentable over Desai *et al.* in view of Madden.

Since the pegylated version of the liposomes are now withdrawn from the present invention, comments relative to GB 2,146,525 and the others as to pegylation are no longer pertinent.

In failing to satisfy the three basis criteria of obviousness, the present invention is patentable over '525 in view of '378 or of '666, thus the invention as claimed in the currently amended form is not made obvious by them..

With these changes and remarks, it is believed that the disclosure is now in condition for allowance and reconsideration is respectfully requested. An early and favorable response is earnestly solicited. Thank you.

Respectfully submitted,



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